

THE SUSCEPTIBLE REGION IN A - V CONDUCTION.

By THOMAS LEWIS, PAUL D. WHITE AND JOHN MEAKINS.

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THE SUSCEPTIBLE REGION IN A-V CONDUCTION.

BY THOMAS LEWIS,* PAUL D. WHITE AND JOHN MEAKINS.

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London.*)

It has been established that auriculo-ventricular heart-block may be produced by direct interference with the main tract of muscular or neuro-muscular tissue which unites the auricles and the ventricles. When the bundle is cut or compressed and the ventricle then fails to respond in normal fashion to the auricular discharges, we see clearly cause and effect. According to our modern conceptions the path through which impulses spread from auricle to ventricle is damaged or broken, and the passage is prevented. In this form of experimental heart-block we have a perfect parallel to those clinical cases of heart-block in which circumscribed lesions are found in the same tract. Clinical heart-block of this form has a clear anatomical cause underlying it.

But there are forms of altered conduction, to use this term in its broadest sense, in which our knowledge is neither so sufficient nor so satisfying. Changes in conduction occur in a variety of circumstances; both as a result of visible injury of the auriculo-ventricular bundle, and with more subtle influences. Thus the rate of conduction is changed physiologically in exercise and with altered heart rate; it is changed from cycle to cycle when extrasystoles are forced from the auricle. Heart-block appears upon stimulation of the vagi. It is caused by the products of asphyxia and by a variety of poisons injected into the circulating blood.

Many questions of importance, both from the theoretical and practical standpoints, arise from these observations. At the present time we shall confine ourselves to one, and shall inquire if we have any knowledge pointing to the special susceptibility of a given region of the heart in respect of the conduction changes considered.

Evidently, a failure of the ventricle to respond to auricular impulses may be explained in a variety of ways; the deficiency may lie in the auricle which fails to supply an adequate impulse; it may be inherent in the junctional tissues and in any part of them; it may be in the ventricles, it being supposed that they lack the power or intermediate means of response. Similar explanations may be applied, with certain qualifications, to simple retardation of conduction. Our inquiry is primarily one of localisation.

* Aided by grants from the Royal Society and Graham Research Fund.

We possess certain preliminary evidences. From the morphological standpoint, the junctional tissues are first suspect; for, as Gaskell states, those tissues which are most capable of rhythmic impulse formation are apparently slowest in conducting the contraction wave, and in the frog and tortoise the *A-V* ring is most susceptible; here there is a natural line of block. It is to the homologues of this ring that we naturally turn in the first instance.

When we consider the mammalian heart our chief evidence lies in the character of the excitation process, portrayed by the galvanometer. The normal ventricular electrocardiogram, or ventricular complex, consists of a number of phases and, according to our present conceptions, the curve as a whole expresses an excitation process which starts and travels in a constant fashion. The normal complex is determined by the response of the ventricle to impulses which descend through well-defined channels; it is the result of a supraventricular impulse, meaning by this term an impulse arising above the level of the main division of the auriculo-ventricular bundle.

Now it is the rule that in heart-block of vagal origin the ventricular complex remains unchanged in quality, though with the altered rate, it may be changed quantitatively. It appears to us in the highest degree improbable that the ventricular complex could thus generally maintain its broad outline, if the susceptible region lay below the level of the chief bundle division; for were the obstruction at a low level two or more points of depression and a simultaneous and equal depression of function in each would of necessity be postulated. The same argument may be applied to other forms of block; *a fortiori* it may be applied to those in which complete block supervenes.

The maintenance* of the physiological ventricular complex in asphyxia, (complete heart-block) in adrenalin poisoning (complete),² in poisoning with strophanthine (partial), digitalis (partial and complete) (personal observations) and in anaphylaxis⁵ (complete) is of significance to our minds and points to a region of the heart above the division of the bundle as the seat of the defect.

Observations.

Our observations were undertaken upon cats, fully anaesthetised with urethane and ether; in all of the experiments the animals were decapitated, and the vagi were divided.

We were led to make the experiments described by previous experiments upon the effect of the vagus on *A-V* rhythm, already reported by one of us (this Journal, page 247); for it appeared from these experiments that the effect of vagal stimulation upon the sequence of chamber contraction is essentially different while *S-A* rhythm on the one hand, and *A-V* rhythm

* We should say perhaps usual maintenance, for in some of the states cited, the normal form may be lost from time to time or experiment to experiment. But this fact does not detract from the force of our argument; the alteration is attributable to a later and less constant effect on the branches of the junctional system.

on the other, predominates. When vagal impulses affect the heart beating in response to an *S-A* rhythm, the usual or *forward* type of heart-block is alone seen. When, on the other hand, an *A-V* rhythm is established, vagal stimulation produces reversed block, that is to say the auricle lags and may fail to respond, while the ventricle is apparently unaffected in this respect. It seemed from these observations that the chief seat of changed conduction lies, during vagal stimulation, in the *A-V* node and predominately to the auricular side of the impulse source. A separate series of experiments* upon extrasystoles carried out by two of us (Lewis and White) has led us to a similar conclusion in regard to the changes of conduction which occur as accompaniments of this form of cardiac disturbance. The view that the *A-V* node or immediately neighbouring tissue forms a susceptible point, so far as changes of conduction are concerned, appealed to us and we have sought and found strongly confirmatory evidence in the effects of asphyxia. Our procedure has been constant in each series of experiments. We produce changes in conduction by some form of interference and test the effect of dislocating the pacemaker from *S-A* to *A-V* node upon these changes of conduction. We anticipated that should the susceptible point be the same for vagal stimulation and for asphyxia we should obtain with the latter, not the ordinary effect of forward block, but reversed block. This anticipation has been fulfilled. The curves of asphyxia in cats need little description, they have been fully illustrated by Lewis and Mathison.³ The curves of simple asphyxia in the present series were similar in every respect. After one or a few minutes of asphyxia, prolongation of the *P-R* interval is seen and is quickly complicated by missed ventricular responses; eventually auricular and ventricular rhythms become completely dissociated.

In producing *A-V* rhythm we have utilised cold applied to the sulcus terminalis and have taken repeated control curves during the course of an experiment, to ascertain the constancy of the reaction of the natural pacemaker to cooling. In these curves cooling is followed by slowing and by an abrupt change of mechanism, from the usual sequence to simultaneous beating in which the auricle slightly precedes the ventricle (Fig. 2*a*).

If, in the cat, *A-V* rhythm is established and maintained, the effects of asphyxia are as follows: In the initial stages of asphyxia the auricle usually beats immediately before the ventricle and the *P-R* interval is conspicuously curtailed. As asphyxia proceeds, the auricular and ventricular systoles become quite synchronous, so that *P* is lost in *R* (Fig. 2*b*, last cycle); after a little while *P* creeps out upon the far side of *R* and an *R-P* interval is developed (Fig. 3 and 1 *a*, *b*, *c*). This *R-P* interval gradually increases (Fig. 1 *a*, *b*, *c*, 4 *b*, and 5) and eventually the auricle fails constantly to respond. A condition is now established for a short while in which the auricle beats at exactly half the rate of the ventricle (Fig. 1 *d* and 5), and this condition may be identified readily by simple inspection of the heart. Finally and

* Subsequently to be reported.

abruptly, all signs of auricular contractions disappear, both from the curves and upon inspection of the heart; yet at the change there is no alteration of ventricular rate.

We have also made a number of observations in which the origin of the impulses was changed at a given phase of heart-block. The transitions vary according to circumstance. Speaking generally they are as follows:

1. If the cold is applied before the development of a long *P-R* interval, then simple *A-V* rhythm becomes established (Fig. 2*a*), having the same time relations as in the controls.
2. If it is applied while the *P-R* interval is prolonged, then the action of auricle and ventricle becomes simultaneous, or *P* follows *R* (Fig. 4*a*).
3. If applied in the early stage of forward 2 : 1 block, then a long *R-P* interval is shown, but the auricle responds at each cycle.
4. If at a later stage, 2 : 1 reversed block is seen.
5. If applied during the final stage of complete dissociation, then the ventricular rate remains practically unaltered, but the auricle ceases to beat.

If, in simple asphyxia and after the development of a given grade of forward block, ventilation is re-established, generally speaking the heart recovers; it recovers gradually and shows the same grades of heart-block as during the induction stage, but in the reverse order. The same statement applies to the reversed block of asphyxia while the heart beats from the *A-V* node. Again, if the cold is withdrawn at any stage of an observation, the corresponding grade of forward block is quickly established. Thus, in Fig. 6, the first portion of the curve shows ventricular cycles only: the auricle has ceased to beat. The cold being withdrawn the normal auricular contractions return and complete dissociation is seen to be established.

Our chief observation is the contrast between the reaction of the heart to asphyxia when *S-A* rhythm and *A-V* rhythm prevail. In the first, forward heart-block develops; in the last, reversed block. The degrees of block in one or other circumstance are not very dissimilar; though it may be said that they are of a lesser order at a given time after the onset of asphyxia if *A-V* rhythm prevails. Thus 2 : 1 forward block gives place to a long *R-P* interval at the transition from one mechanism to the other in most instances. This is due in part at least to the relatively lower rates of impulse formation in the *A-V* node. The *S-A* node is depressed in the simple asphyxia at or almost at the time when block develops; the *A-V* node reacts to asphyxia in similar fashion.

The disappearance of the auricular responses to an *A-V* rhythm at a late stage of asphyxia is readily explained. It occurs at the stage of complete block, and the impulses fail to reach the auricle. The auricle is robbed of the *S-A* impulses by the application of ice-cold water to this node. It is guarded

from the *A-V* impulses by the block induced by asphyxia. Cut from its two chief sources of impulses it remains absolutely quiescent. It is necessary for us to state that our observations allow us to draw this last conclusion for the asphyxial state only. We know that both *S-A* and *A-V* rhythms are depressed by continued asphyxia, and it may be that hypothetical centres in other parts of the auricle might suffer similarly or in greater degree; so that although they do not become automatic in asphyxia when *S-A* and *A-V* nodes are thrown out of action, they might yield auricular responses under more normal conditions of nutrition.

Our observations in a measure affect the conclusions to be drawn from v. Ángyán's¹ observations, made some while since in this laboratory. v. Ángyán used the complete heart-block of asphyxia to test the effect of vagal stimulation upon the idioventricular rhythm. In the light of our present results, we now know that what has been termed idioventricular rhythm for the mammalian heart in the past, namely, the rhythm which governs the dissociated ventricle, may arise in the *A-V* node.* A rhythm of this kind springs from a different centre than that which develops automaticity when the *A-V* bundle is cut or compressed. When *A-V* rhythm is maintained and heart-block is developed as a result of asphyxiation the auricle alone shows abrupt changes of rate. The fall of rate in the ventricle is steady and progressive until after the establishment of complete block and at the time of its establishment shows no further alteration. The rhythm controlling the ventricle is propagated therefore from one centre throughout. The same statement applies to the ventricular rhythm when there is a change from *A-V* to *S-A* rhythm or vice versa, during the complete heart-block stage (Fig. 6). The *A-V* node controls the ventricle therefore in the complete heart-block of asphyxia. v. Ángyán's results are in reality the results of vagal stimulation upon *A-V* nodal impulses; therefore, they are not strictly comparable to the similar observations of Hering and Erlanger who dealt with dissociation at a lower level of the heart.

In the late stage of simple asphyxia in cats, namely after the appearance of complete dissociation, the auricular contractions almost always disappear; the change is abrupt and does not affect the rhythm or rate of ventricular contraction. When this happens the heart will not recover although re-oxygenated. The explanation of this phenomenon is not difficult. It is due to abrupt termination of the function of the *S-A* node, the *A-V* node continuing to control the ventricle. This change would account fully for the end curves of simple asphyxia in the cat and incidentally for certain of the curves of the dying human heart published by Robinson.⁴

* It is probably as a result of a high level block that the greater rate of the ventricle in complete heart-block induced in the human subject by digitalis or its allies is due. We have attempted to test the level of block in strophanthine poisoning in cats, using repeated injections of 1/800 grain. But it has not been found possible owing to the extraordinary reaction of the *S-A* node to this drug. After the injections, and at a stage when heart-block was present, we have found repeatedly that cold has little or no effect on the *S-A* node.

CONCLUSIONS.

1. While asphyxia produces a gradually increasing *forward* heart-block in the cat's heart beating from the *S-A* node, it produces a gradually increasing reversed heart-block when the heart chambers respond to the *A-V* node. From this we may conclude that in asphyxia the susceptible region in respect of changed conduction is the *A-V* node itself or tissues in its immediate vicinity. The main defect is in a portion of the junctional system lying at a higher level (nearer the auricle) than the actual seat of impulse discharge in *A-V* rhythm. This conclusion applies, in the cat, to rhythms in which the *P-R* interval is reduced to a small fraction of its original value.*

2. Considering the results of the experiments here reported, and of similar experiments upon the effects of vagal stimulation and of extrasystoles† upon conduction in *S-A* and *A-V* rhythms, we are of opinion that the *A-V* node or tissue in its immediate vicinity is the most susceptible tissue in respect of changes in *A-V* conduction.

3. In the cat, so asphyxiated that there is a complete functional break between *A-V* node and auricle, the application of cold to the *S-A* node brings about standstill of the whole of the auricular tissue.

4. The effects of vagal stimulation in the automatic ventricle, as reported by v. Ángyán, are regarded as the effects of vagal stimulation upon the *A-V* rhythm, for in the complete block of asphyxia the dissociated ventricle is controlled by the *A-V* node.

5. When at the end of a simple asphyxia of the cat the auricular contractions disappear abruptly during the stage of complete *A-V* dissociation, this change is attributable to depression of the pacemaker, the *A-V* node continuing to control the movements of the ventricle.

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- ² KAHN. Archiv. f. d. ges. Physiol., 1909, CXXIX, 379.
- ³ LEWIS AND MATHISON. Heart, 1910-11, II, 47.
- ⁴ ROBINSON. Journ. of exper. Med., 1912, XVI, 291 (Fig. 2).
- ⁵ ROBINSON AND AUER. Journ. of exper. Med., 1913, XVIII, 548; (see also AUER AND ROBINSON, *ibid.*, XVIII, 435).

* In the dog the level at which the impulses form appears to be variable. In the cat, we have not seen slight reduction of the *P-R* interval, the reduction has always been conspicuous.

† Observations reported in an accompanying paper and in a paper to appear shortly.

Electrocardiographic curves from cats, illustrating the effects of asphyxia upon *A-V* rhythm. All curves are from Lead *II*. Abscisse 2 seconds, ordinates 2×10^{-4} volts.

Fig. 1 (a), (b), (c), (d). A series of curves from a single asphyxial period.

(a) Commences 2 minutes after ventilation ceased. The original *P-R* interval was .075 seconds; here it is .093 seconds. The curve shows the effect of cold applied to the sulcus at this stage of asphyxia. There is profound slowing and *A-V* rhythm becomes established, *P* and *R* falling together. In control curves without asphyxia, the auricular contraction appears .013 seconds before *R* during *A-V* rhythm. A slight grade of reversed block is already present therefore in the end beats of this curve.

(b) Taken after 2 minutes 25 seconds of apnoea. *P* appears to the right of *R*. The simple asphyxial control showed 2:1 forward block at this stage.

(c) After 2 minutes 40 seconds. The *R-P* interval has increased further. The simple asphyxial control showed 2:1 forward block at this stage.

(d) After 3 minutes 30 seconds. 2:1 reversed heart-block is shown, the invert *P* appearing well after *R*, but at alternate cycles only.

Fig. 2 (a). A control curve showing the effect of applying cold to the sulcus terminalis. The curve was taken at the commencement of apnoea. The heart slows and the normal sequence gives place to simultaneous contraction of auricle and ventricle. The auricular deflection immediately precedes *R* during the *A-V* rhythm.

Fig. 2 (b). 60 seconds later in the same asphyxia. The curve shows the commencement of reversed block; the *P-R* interval becomes reduced until *P* passes into *R* and is hidden by it.

Fig. 3. 45 seconds after the onset of asphyxia, cold was applied. The heart slows and *A-V* rhythm becomes established; almost simultaneously heart-block begins to be manifest. *P*, which is at first synchronous with *R*, gradually creeps out to the right of it.

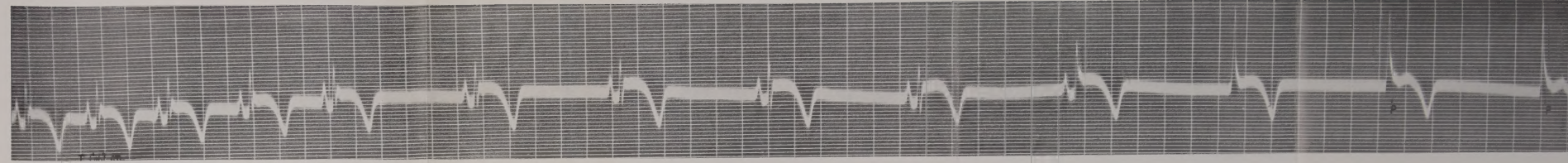


Fig. 1a.

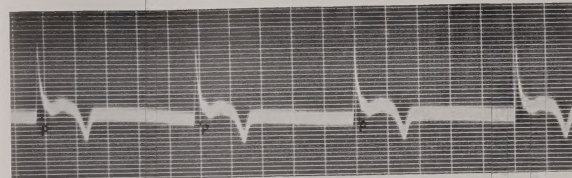


Fig. 1b.

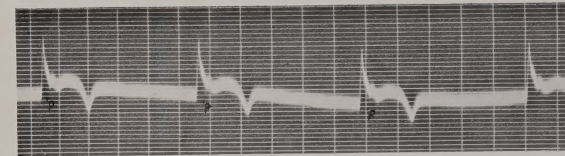


Fig. 1c.

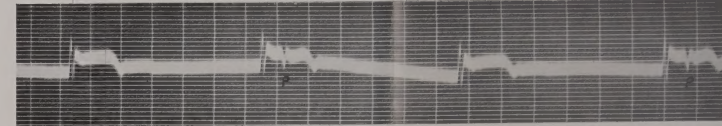


Fig. 1d.

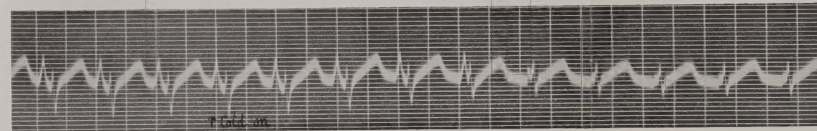


Fig. 2a.

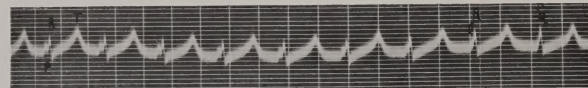


Fig. 2b.

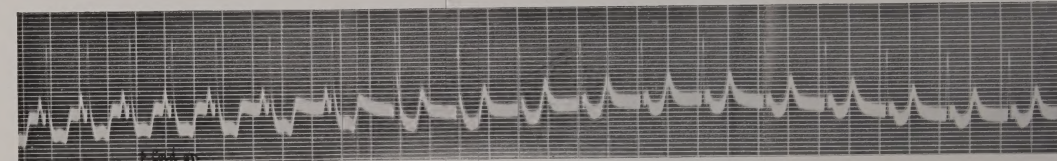


Fig. 3.

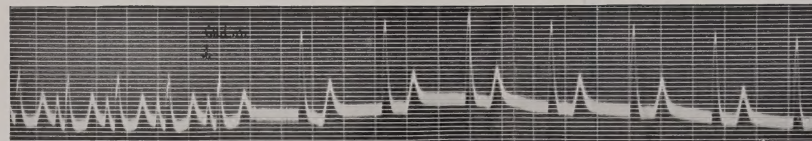


Fig. 4a.

Fig. 4 (a). Cold applied 50 seconds after the onset of asphyxia and at a time when slight prolongation of the *P-R* interval had appeared. *A-V* rhythm becomes established, *P* and *R* being simultaneous.

Fig. 4 (b). A period of 4 seconds has elapsed between this curve and the last. The present figure shows the development of reversed block; i.e. gradual prolongation of the *R-P* interval.

Fig. 5. A curve, commencing 90 seconds after the withdrawal of artificial respiration; cold being applied to the sulcus throughout. The auricular deflection lies at first on the downstroke of *R*. As asphyxia proceeds, it retreats gradually from *R*; late in the curve dropped beats are evident and finally 2:1 reversed heart-block, in which the ventricular rate is double the auricular, becomes established.

Fig. 6. After establishing *A-V* rhythm by applying cold continuously, a cat was asphyxiated; by the 145th second of asphyxia the heart had passed through several stages of partial reversed block and finally the auricular contractions had vanished. The curve commences at this state and shows the recovery of the *S-A* node soon after the withdrawal of cold from it. The ventricular rate is practically unaltered and complete heart-block is evidenced by the dissociation of auricular and ventricular rhythms.

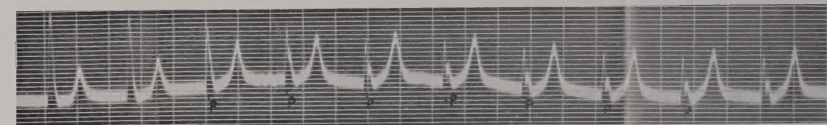


Fig. 4b.

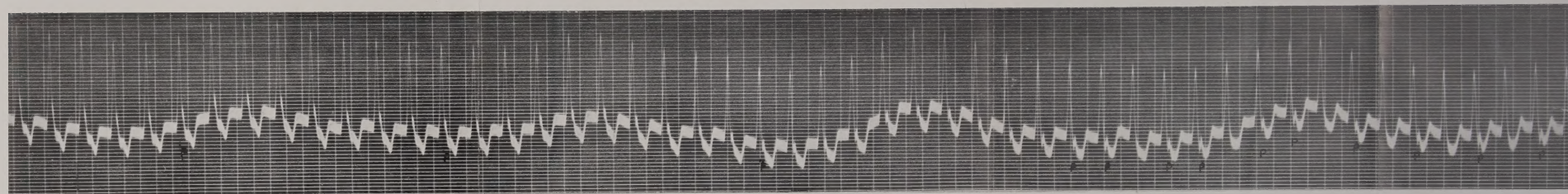


Fig. 5.

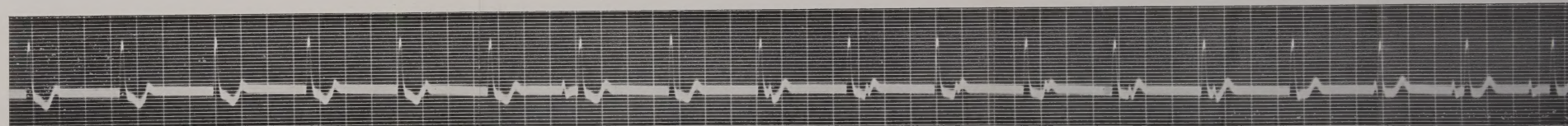


Fig. 6.

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